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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,779	07/02/2002	Anders Dahlqvist	0093/000003	7114

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EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,779	DAHLQVIST ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-57* is/are pending in the application.

4a) Of the above claim(s) *52,53,56 and 57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,51,54 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/14/05;9/28/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

2. Applicant's response to the Communication mailed May 9, 2006 on June 8, 2006, is acknowledged. Applicant's response to the Office Action mailed July 13, 2005 on November 14, 2005 and the Office Action mailed on February 2, 2006 on March 2, 2006 is acknowledged.

Claim Disposition

3. Claims 1-49 have been canceled. Claims 50-57 have been added. Claims 50-57 are pending. Claims 50-51 and 54-55 are under examination. Claims 52-53 and 56-57 are withdrawn as directed to a non-elected invention. As previously stated in the communication on February 2, 2006, the newly submitted claims 52-53 and 56-57 are directed to an invention that is independent or distinct from the invention elected on April 21, 2005. It is noted that the Amendment filed on November 14, 2005 on page 12 indicated that applicant would now like to pursue SEQ ID NO:5, however, SEQ ID NO:1 and 2 was elected and examined. Since applicant has received an action on the merits, this invention has been constructively elected and claims 52-53 and 56-57 are withdrawn. Claims 50-51 and 54-55 are only examined to the extent that they pertain to the elected subject matter.

Information Disclosure Statement

4. The information disclosure statement (IDS) filed September 28, 2001 has been considered and the PTO-1449 form is attached. However, the IDS filed on November 14, 2005 fails to comply with 37 CFR 1.98(a)(2), because the references are incomplete citations, no dates or authors appear. In addition, Accession Nos. SPBC776 and AI398644 are duplicates of references submitted on the September 28, 2001 IDS.

Compliance with Sequence Rules

5. The sequence amendment filed on June 8, 2006 has been received and entered.

Priority

6. As previously stated, the instant application is granted the benefit of priority for the U.S. provisional Application No. 60/180687 filed on February 7, 2000 as requested in the declaration. The instant application is granted the benefit of priority for the foreign application 99106656.4 filed in the European Patent Office on April 1, 1999 and foreign application 99111321.8 filed in the European Patent Office on June 10, 1999 as requested in the declaration. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d) or (f), which papers have been placed of record in the file.

Withdrawn-Specification Objections

7. Previous objections to the specification is withdrawn by virtue of submission of an amendment.

New- Specification Objections

8. The specification is objected to because of the following informalities:

The specification is objected to because the first paragraph on page 1 does not contain a complete priority statement, for example, "This application is a 371 of PCT/EP00/02701, filed March 28, 2000 which claims benefit to U.S. Provisional Application Number 60/180,687, filed February 7, 2000 and claims benefit under 35 U.S.C. 119 (a-d) to foreign application 99106656.4 filed in the European Patent Office on April 1, 1999 and foreign application 99111321.8 filed in the European Patent Office on June 10, 1999".

It is noted that the amendment filed on June 8, 2006 amended the specification to add SEQ ID NO:32 on page 3 of the specification. It appears that the amendment also corrected a typographical error that appeared on line 29 of page 3, however, the correction was not annotated with underlining. See page 3 of the original specification where the word "furthermore" is misspelled as "furtherm" and the corrected paragraph has the proper spelling but the word is not underlined. Applicant is reminded that amendments made to the instant application are to annotate with a strike out line if deleted or underlined if added.

Correction is required.

Withdrawn-Claim Objections

9. Previous objections to the claims are withdrawn by virtue of submission of an amendment.

New-Claim Objection

10. Claims 50-51 and 54-55 are objected to because of the following informalities:

Claim 50 is objected to because the sequence notation is improper, see "SEQ ID NO.1" which should be "SEQ ID NO:1". In addition, item (a) is confusing with the recitation of "i) to iv)", it is suggested that the claim is amended to read, "a) a nucleotide sequence under conditions whereby said nucleotide sequence is:" and delete "is" in items (i-iv). In addition, claim 50 is objected to because the following appears "acyltranferase" which should be "acyltransferase".

It is noted that the claim language represents a Markush within a Markush, however, the claim language is not consistent. For consistency of claim language it is suggested that the claim is rewritten as follows:

A process for the production of triacylglycerol, comprising growing a transgenic cell or transgenic organism comprising one or more of the following:

A) a nucleotide sequence under conditions whereby said nucleotide sequence is:

(i) a nucleotide sequence as set forth in SEQ ID NO:1 or a homologous nucleotide sequence, which is at least about 40% identical to a nucleotide sequence of SEQ ID NO:1;

(ii) a nucleotide sequence or a homolog thereof which is at least about 40% identical to a nucleotide sequence selected from the group consisting of sequences as set forth in SEQ ID NO:1, 3....30 and 31, or a homolog encoding an amino acid sequence for an enzyme or an isoenzyme or a functional fragment thereof;

(iii) a partial nucleotide sequence which corresponds to a full length nucleotide sequence selected from the group consisting of sequences as set forth in SEQ ID NOS:5...or 31, or a homolog thereof; and

(iv) a nucleotide sequence, which is at least 40% identical to a nucleotide sequence selected from the group consisting of those sequences set forth in SEQ ID NOS:1...30 and 31, is expressed;

(B) a gene construct comprising a nucleotide sequence (A), operably linked to a heterologous nucleic acid, and

(C) a vector comprising a gene construct (B), or a nucleotide sequence (i), wherein the activity of the enzyme (ii) is acyl-CoA independent. It is suggested that the similar amendments are made to claim 51 to clarify the claim language.

Claims 51 is objected to because the sequence notation is improper, see "SEQ ID NO.1" which should be "SEQ ID NO:1". In addition, items (a-d) and items "(i-iii) are confusing with the recitation of "is", it is suggested that the claim is amended to delete "is" in all items. Claims 54-55 are objected to for the recitation of "isolating triacylglycerol" because the article "the" is missing from the claims. It is suggested that the claims are amended to read, "isolating the triacylglycerol".

Correction is required.

Withdrawn-Claim Rejections - 35 USC ∋ 112

11. Previous rejection to claims under 35 U.S.C. 112, second paragraph, are withdrawn by virtue of submission of an amendment.

Maintained and Amended-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 50-51 and 54-55 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a process for the production of triacylglycerol comprising growing a transgenic cell or organism comprising one or more nucleotide sequence: (i) a nucleotide sequence set forth in SEQ ID NO:1 or a homologous nucleotide sequence at least 40% identical to SEQ ID NO:1; (ii) a homolog encoding an amino acid sequence for an enzyme or an isoenzyme or a functional fragment thereof etc. (see claim 50 for example). Thus, the claims encompass a large variable genus and the instant specification lacks adequate written description for the genus of nucleotides related to SEQ ID NO: 1.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which

is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (see *Enzo Biochemical*, 63 USPQ2D 1609, CAFC 2002).

University of Rochester v. G.D. Searle & Co. (69 USPQ2d 1886 (2004)) specifically points to the applicability of both *Lily* and *Enzo Biochemical* to methods of using products, wherein said products lack adequate written description. While in *University of Rochester v. G.D. Searle & Co.*, the methods were held to lack written description because not a single example of the product used in the claimed methods was described, the same analysis applies wherein the product, used in the claimed methods, must have adequate written description as noted from Enzo Biochemical (see above).

On pages 20 and 28-29 of the instant specification, nucleotide sequences from five species for genes encoding phospholipid:diacylglycerol acyltransferase (PDAT) are disclosed, including the PDAT gene from *Saccharomyces cerevisiae* which has a structure described by SEQ ID NO: 1. Applicants have described structural features of the PDAT gene from *Saccharomyces cerevisiae* of SEQ ID NO: 1; however, a description of the genus of genes that are at least 40% identical to SEQ ID NO: 1 or a homolog thereof which is at least about 40% identical to SEQ ID NO:1", is lacking. It is noted that claim 50 for example has been amended to recite, "wherein the activity of PDAT acyltransferase catalytic activity is acyl-CoA independent",

however, there is no nexus between the "wherein clause" and the preamble of the claim. In addition, the "wherein clause" does not garner a function for the entire genus of homologs claimed. A skilled artisan cannot envision the detailed chemical structure of the genus encompassed in the claims or be able to predict the structure of other members of this genus by virtue of the instant disclosure. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the

complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

13. Claims 50-51 and 54-55 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for growing yeast and *Arabidopsis thalliana* in which a gene described by SEQ ID NO: 1 is expressed, does not reasonably provide enablement for the genus of processes wherein any transgenic cell or transgenic organism is grown in which any homolog of SEQ ID NO. 1 is expressed (claim 50, for example) or any use of any homolog of SEQ ID NO: 1 for producing triacylglycerol (claim 50, for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The amount of experimentation required of one of skill in the art to use the claimed invention to the full extent of its scope is undue.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as

routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988)*. The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue. The specification contains one working example of a transgenic cell and one example of a transgenic organism that can be used to make triacylglycerol: yeast that express SEQ ID NO: 1 and *Arabidopsis thaliana* that express SEQ ID NO: 1. Applicants, however, present no guidance or working examples of the use of the genus of transgenic cells and transgenic organisms or the genus of nucleotides included in the scope of the claims, which also reads on human beings. The nature of the invention is such that SEQ ID NO: 1 encodes a functional protein, a phospholipid:diacylglycerol acyltransferase (PDAT), which catalyzes the transfer of

phospholipids to diacylglycerol; and with a deviation from the known sequence, the predictability of functionality becomes extremely low. The predictability of making isolated nucleotides that encode polypeptides as little as 40% sequence identity to SEQ ID NO: 1 which also maintain the function of PDAT can be increased by comparing the sequences of a genus of known PDAT's to SEQ ID NO:1 and identifying important/conserved residues; however, the specification discloses only a few examples nucleotides that encode PDAT's. The state of the prior art is such that a comparison of a sufficient number of sequences of PDAT's to the disclosed PDAT from *Saccharomyces cerevisiae* cannot be performed. In addition, the nature of transgenic organisms is that they are unstable and difficult to make; to make all of the transgenic organisms that express molecules related to SEQ ID NO: 1 included in the scope of the claims is wholly unpredictable. The breadth of the claims and the unpredictability of the art render the instant claims not enabled to the full extent of their scope without undue experimentation.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of

success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected. The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable. The skilled artisan would recognize the high degree of unpredictability that all the fragments/variants encompassed in the claims would retain the recited function.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) disclose two polypeptides having 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Fig. 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Fig. 3), however, these polypeptides exhibit distinct functions. The modifications exemplified in the Seffernick et al. reference is small compared to those contemplated and encompassed by the claimed invention.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed genus. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct all of the genus of the claimed invention and examine the same for function.

The specification does not provide support for the broad scope of the claims. The claims broadly read on any transgenic organism or transgenic cell and any homolog thereof for the given sequence (SEQ ID NO: 1). The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to

scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test the large variable genus of products of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possibilities and to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

14. Claims 50 and 54 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 50 is indefinite for the recitation of

Claims 50 lacks clear antecedent basis for "the activity of PDAT acyltransferase catalytic activity is acyl-CoA independent" as the claim language prior to this statement does not refer to the enzyme designated as phospholipids:diacylglycerol acyltransferase (PDAT) or the activity of catalyzing in an acyl-CoA independent reaction the transfer of fatty acids. Dependent claim 54 is also included in this rejection as it does not rectify the deficiency. In addition, the method claimed in claim 50 is open ended, as the recited "wherein clause" does not close the method. The "wherein clause" does not demonstrate the product (triacylglycerol) in hand or demonstrate that the objective in the permeable is achieved. It is noted that claim 54 recites isolation of the product (triacylglycerol), however, claim 50 needs to stand on its own.

New-Basis For NonStatutory Double Patenting (based on successive amendments made to the claims in the instant application and the copending application)

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 50-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-32 of copending application number 09/537,710. An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). *See In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).* Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant application claim is directed to a process for the production of triacylglycerol comprising growing a transgenic cell or organism comprising one or more nucleotide sequence: (i) a nucleotide sequence set forth in SEQ ID NO:1 or a homologous nucleotide sequence at least 40% identical to SEQ ID NO:1 etc. (see claim 50 for example). The copending application claims are directed to a process for the production of triacylglycerol comprising growing a transgenic cell or transgenic organism which contains a nucleotide sequence SEQ ID NO:1 from *S. cerevisiae* or a nucleotide encoding SEQ ID NO:2, DNA which is at least 95% identical to

SEQ ID NO:1 whereby the nucleotide sequence encoding an enzyme is expressed, wherein said enzyme catalyzes in an acyl-CoA-independent reaction the transfer of fatty acids from phospholipids to diacylglycerol in the biosynthetic pathway for the production of triacylglycerol and transgenic cells comprises an enzyme which catalyzes in an acyl-CoA-independent reaction the transfer of fatty acids from phospholipids to diacylglycerol in the biosynthetic pathway for the production of triacylglycerol. The two sets of claims differ as the copending claim recites "the actual process steps to produce the triacylglycerol, for example the transfer of fatty acids" and the copending claims recite the source of the sequence and the encoding enzyme structure. In addition, the copending application differs as the claims recite at least 95% identity to SEQ ID NO:1. However, the specification of the instant application states that the source of SEQ ID NO:1 is *S. cerevisiae* and SEQ ID NO:2 is also disclosed in the instant specification (see page 3). Furthermore, the instant specification discloses the actual process steps that lead to the desired product, triacylglycerol which involves the transfer of fatty acids and the objective of the method is the production of triacylglycerol. Additionally, the instant claims recite the percent language of "40% identity" as an alternative as does the copending application pertaining to the recited "95% identity". Therefore, the two sets of claims are an obvious variations of each other as the instant claims recites a genus and the copending application recites a species.

Although the scope of the claims herein differs, the two sets of claims are directed to similar inventions as the claim language has the same material. One of ordinary skill in the art would be motivated to modify the instant claims to recite, for example the species that is contained in the genus as disclosed in the instant specification and one of which is recited in the copending application claim because it clarifies the claim by providing the specific species.

Thus, the copending claims are an obvious variation of the instant application claim, therefore *prima facie* obvious.

This is a provisional obvious-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 50 and 51 are rejected under 35 U.S.C. § 102(b) as being anticipated by WO 98/55631 (Lardizabal *et al.*, see IDS, September 28, 2001) based on the broad recitation of "a homologous nucleotide sequence which is at least about 40% identical or a homolog thereof". The instant claims are drawn to methods of producing triacylglycerol (triglyceride) by growing transgenic host cells expressing a nucleotide sequence that is homologous to SEQ ID NO: 1.

Lardizabal *et al.* teach transgenic host cells that express nucleic acids encoding diacylglycerol acyltransferases (DAGAT) to modify triacylglycerol levels (see page abstract and page 61). Expressing DAGAT inherently increases triacylglycerol production because DAGAT catalyzes the formation of triacylglycerol from fatty acyl-CoA and diacylglycerol substrates. In the broadest reasonable interpretation of the claims, DAGAT is a homolog of PDAT because,

like PDAT, it is a diacylglycerol acyltransferase (claim 50, see page 637, column 1). In addition, the reference discloses on page 25 the utilization of long chain fatty acids and other chain lengths in the method (claim 51). Thus, Lardizabal *et al.* anticipate claims 50 and 51.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 50 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson *et al.* (see PTO-892) in further in view of Genbank Accession Entry X77395 (see PTO-892). The instant claims are drawn to methods of producing triacylglycerol (triglyceride) by growing transgenic host cells expressing a nucleotide sequence that are homologous to SEQ ID NO: 1.

Genbank Accession Entry X77395 teaches the open reading frame that encodes *S. cerevisiae* phospholipid:diacylglycerol acyltransferase (PDAT) (identified as N2042). This reference does not teach the DNA molecule in vectors with selectable markers, host cells, or in a process for producing transgenic cells.

Watson *et al.* teach the usefulness of investigating encoded proteins from their respective genes using vectors with selectable markers, host cells, and transformations into plant cells of plants (see pages 99, 119-23, 235-9, 273-4 and 281-5). It would have been be obvious to one of ordinary skill in the art at the time the invention was made to use the DNA disclosed in the above

reference in vectors with selectable markers, host cells, and processes for producing transgenic cells because the references specifically disclose open reading frames of genes which encode proteins. The motivation for such experiments is found in the Preface of Watson *et al.*, which states that "the great power of recombinant DNA techniques comes from the ability to explore gene function by manipulation of genes and then introducing them back into cells" to bring about our understanding of living organisms". The Examiner suggests adding the step of isolating triacylglycerol to the methods of claims 46 and 48 to overcome the rejection.

Response to Arguments

19. The response filed on March 2, 2006 and November 14, 2005 have been considered. Note that the rejections of record under 35 U.S.C. 112, first paragraphs, 102 and 103 have been maintained, however, are amended based on the amendments made to the claims. On page 4 of the amendment filed on March 2, 2006, applicant state that the specification must only describe the invention in sufficient detail so that one skilled in the art can clearly conclude that the inventor invented the claimed invention. Applicant cites *Lockwood v. American Airlines, Inc.* and *In re Wertheim* in support of said statement. In addition, applicant cites the MPEP, stating that "a representative number of species does not require the description to be such specificity that it would provide individual support for each species that the genus embraces and such, a single species may be enough to identify the entire genus". Applicant asserts that the instant specification fully complies with these requirements. This argument is not persuasive. Applicant is reminded that a representative number of species is required to adequately describe the claimed genus. A representative number of species means that the species, which are

adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. The instant specification fails to provide a representative number of species of the claimed genus. In addition, adequate description is required for the homologs thereof and structures that are at least about 40% identical to SEQ ID NO:1, for example, what residues are conserved or what variations can be tolerated by the structure to preserve function.

Applicant opines that the claims have been rewritten in such a way that the problems described by the examiner in the office action no longer apply. It is further stated that applicant has provided five sequences of PDAT genes, which provide exemplifications of the instant invention when not even a single example is required. Thus applicant concludes that adequate written description is provided (see pages 4-5 of the response). This argument is not persuasive because the claims are still drawn to large variable genus based on the language "a homolog thereof" or "a sequence that is at least about 40% identical to SEQ ID NO:1" which can be interpreted as "33%, 34%, 35%, 36%,37%, 38%, 39%, 40%, 41%, 42%, 43%, 44%, 45%" for example, and there is no indication of where in the sequence modifications will occur and if said modifications can be tolerated or what regions are conserved. Therefore, the genus issue raised in the previous office action remains, and applicant's statement that the claims as rewritten are no

longer problematic is incorrect. Further, the genus encompassed in the claims is very large and variable, thus the exemplification provided is not representative of the large variable genus. The sequence in question is SEQ ID NO:1, which is disclosed as having 1986 nucleotides, thus 794 nucleotides is homologous to SEQ ID NO:1 based on the 40% identity limitation claimed. The 794 nucleotides do not have to be contiguous and there is no indication of conserved regions. Applicant's arguments have been considered in full, however, are not persuasive because the claims encompass a large variable genus as stated above and herein. Thus, the rejection remains.

Regarding the enablement rejection, applicant on page 5 states that the specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without undue experimentation. Applicant further states that the claims as currently amended are fully enabled by the specification of the instant application in combination with the general knowledge of one of ordinary skill in the art. Applicant cites *Amgen Inc. v. Hoechst Marion Roussel, Inc.* and *Capon* in support of their arguments. Applicant's arguments are not persuasive because the claims encompass a large genus and to make and test all the species included in that genus to determine if they have function or the desired activity would require undue experimentation. Furthermore, with regard to applicant's statements about the knowledge in the art, note that Seffernick et al. as stated above disclose two polypeptides that have 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids, however, these polypeptides exhibit distinct functions, although they are identical along relatively long stretches of their respective sequences. Note that the variation contemplated in the instant application is far greater than what was exemplified in the Seffernick

et al. reference. It is noted that the protein in the art is different from the instant application, however, applicant is relying on the general knowledge in the art to substantiate the claimed variability in structure of the instant products. Thus, the claimed invention is highly unpredictable in view of the disclosure in the art. Therefore, the instant specification does not provide support for the breath of the claims.

Applicant also state that the skill in the art at the time of filing was such that creation of transgenic organisms, in general, was routine. Note that the claims broadly recite growing a transgenic cell or organism, which encompasses, humans. The instant specification exemplifies a plant, thus, clearly, the specification is not commensurate in scope with the claims. No correlation is made between structure and function, for example where in the 1986 nucleotides will the 794 nucleotides (that represent 40% sequence identity) be positioned. No requirement is made for conserved regions, or a contiguous run of nucleotides. The claims read on a structure that has the first 794 nucleotides or a structure that has the last 794 nucleotides or 794 nucleotides in the middle of the sequence or 794 nucleotides throughout the sequences that are not contiguous or 794 nucleotides wherein a few nucleotides are contiguous and the rest are not, and the possibilities can go on. Absent guidance in the specification, the skilled artisan would have to make all the possibilities and test them to find a sequence as claimed with the desired activity. Thus, the rejection remains.

The response filed on November 14, 2005 has been considered, however, is not persuasive. On page 13 of this response it is stated that the Lardizabal et al. reference cited under 35 U.S. C. 102(b) does not suggest or teach numerous recitations of the independent claims. It is further stated that the instant invention discloses that catalysis occurs with the transfer of fatty

acids from phospholipids to diacylglycerol in the production of triacylglycerol through an acyl-CoA independent reaction. This argument is not persuasive. In fact, applicant is arguing limitations that are not evidenced by the present claim language. For example, claim 50 recites a process for the production of triacylglycerol by growing a cell or organism that comprises a nucleotide sequence that is defined in the claim (see items a-c and i-iv) and then the claim recites "wherein the activity of PDAT acyltransferase catalytic activity is acyl-CoA independent" and no nexus is made between the wherein clause and the rest of the claim. In addition, the claim does not mention PDAT prior to the wherein clause or its catalytic activity. It is noted that the specification discloses on page 3 that "...it was proved that the disrupted gene encodes a PDAT enzyme (SEQ ID NO:1 and 2). However, the claim does not recite limitations as argued by applicant. In addition, the present language in the claim does not clearly delineate that the wherein clause pertains to the entire Markush listing in claim 50 and it appears to be associated only with item (c). Thus, the claim is interpreted as follows, "...and (c) a vector comprising a gene construct (b), or a nucleotide sequence (i) wherein the activity of PDAT acyltransferase catalytic activity is acyl-CoA independent". Thus, item (i) for example, is anticipated by the reference as written in the alternative. Therefore, applicant's arguments have been considered but are not persuasive, and the rejection remains.

On page 14 of the November 14, 2005 amendment applicant state that the examiner must show in the prior art some suggestion or motivation to make the claimed invention, a reasonable expectation for success in doing so, and a teaching or suggestion of each claim element. It is further stated that applicants added claims 54-57, which recite the isolation of triacylglycerol and applicant concludes that the references singly or in combination do not teach the claimed

invention. This argument is not persuasive. A suggestion was made to add the limitation of isolated to the claims to obviate the present ground of rejection, however, applicant added the limitation in a new dependent claim not the independent claim, thus, the references remain applicable. Further, motivation to combine the references is provided above with a reasonable expectation of success therefore the references remain applicable and the rejection remains.

Note that new grounds of rejections have been made under 35 U.S.C. 112 first paragraph, and Obvious-type Double Patenting based on consecutive amendments made to the instant claims and the claims in the copending application, for the reasons stated above.

Conclusion

20. No claims are allowable.

21. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 7/14/06